REMARKS

Claims 1-3, 10-16 and 45 remain before the Examiner for reconsideration. Claims 4-9 and 17-44 have been canceled without prejudice. Claims 1, 3, 10, 11, 13, 14, 16 and 45 have been amended herein as indicated above. Additions to the claims are indicated by underling the text added, and deletions from the claims are indicated by striking through the text deleted.

In the Office Action dated July 14, 2003, in the above-referenced application, the Examiner withdrew the objection to claim 1 in light of the amendments made by Applicants in the Response filed April 30, 2003. The Examiner also withdrew the rejection of claim 45 over Brenner in light of the amendments made thereto. However, the Examiner indicated that all other rejections were maintained and that a new rejection "necessitated by applicant's amendment" was included in the office action.

In that regard, the Examiner rejected Claims 1, 2, 10, 11, 12, 14, 15 and 45 under 35 U.S.C. 102(e) "as being anticipated by Hochlowski et al (US 6,168,913) as evidenced by Webster's Dictionary (1994)". Specifically, the Examiner asserted that:

> Hochlowski et al discloses "coding combinatorial chemical libraries synthesized on a plurality of solid supports by attaching "tags" that comprise fluorine containing compounds in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine nuclear magnetic resonance spectroscopy..." (see Abstract). Various fluorine containing tags are disclosed by the reference (see column 5, line 15 through column 13, line 21); these read directly on the claimed fluorous {tagging} moieties that differ in fluorous content or structure of instant claims 2, 12 and 15.
>
> The reference discloses using FNMR to identify the tags (see, for example, column 3, lines 2-21 and column 23, lines 1-14), creating for each solid support a code that generates "an unique FNMR spectrum" (column 4, lines 410). Note that for the purposes of this rejection that the term "separating" is given the art-recognized definition of "to discriminate or differentiate between", as evidenced by Webster's Dictionary. Thus, Hochlowski et al discloses "separating" the compounds of their coded libraries as the

> FNMR spectrum *clearly differentiates* between the tagged library members (see, for example, column 23, lines 1-14, Example 2 and patented claims). The separation discussed above is based on differences between the FNMR chemical shifts of the tagging moieties, see column 5, line 15 through column 13, line 21 J especially column 5, line 29) and Figures. This also reads on the "differences in fluorous nature" in instant claims 1, 11 and 14 and also on the "differences between the first tagging moiety and the second tagging moiety" in instant claim 45. Lastly, as the chemical shifts of the tags are known, the "order" of separation (i.e. placement of peaks in the FNMR spectrum) to identify the compounds that are tagged is deemed to be "predetermined", as recited in instant claims 10 and 45.

The Examiner further asserted that Applicants' arguments filed April 30, 2003 in regard to the above were not persuasive. Specifically, the Examiner asserted that:

> Applicant argues that the terms "separating" or "separation" should be given a special meaning (from a chemical dictionary). Applicant has not pointed to any place in the instant specification that supports such a definition. Moreover, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).
>
> The examiner has given the claims their broadest reasonable interpretation and maintains that Hochlowski et al reads on the claimed invention as described in the rejection above.
>
> In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., special meaning (from a chemical dictionary) of "separating" or "separation") are not recited in the rejected claim(s). If applicant intends for "separating" or "separation" to be limited to a particular meaning, that limitation should be added to the instant claims.
>
> See also MPEP 2111.01: During examination, the claims must be interpreted as broadly as their terms reasonably allow. This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. *In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Applicants respectfully traverse the Examiner's rejection.

Once again, Hochlowski et al. discloses a method encoding combinatorial chemical libraries synthesized on a plurality of solid supports (a polymeric beads) by attaching tags to the solid supports that comprise fluorine containing compounds. The tags can be decoded while attached to the solid support/polymeric bead by fluorine nuclear magnetic resonance (FNMR) spectroscopy to follow the reaction history of individual beads and to determine the particular member of the library that is attached to the polymeric bead.

Unlike the present invention and contrary to the Examiner's assertion, nowhere does Hochlowski et al. disclose or suggest a physical separation of the polymeric beads (or any other entity) based upon differences in the tags attached thereto. Given the extremely high molecular weight of such polymeric beads, there is no known separation technique via which a physical separation could be accomplished based upon differences in the tags attached thereto. FNMR spectroscopy can be used only to identify different polymeric beads based upon different encoded tags. Because the polymeric beads of Hochlowski et al. are quite large, they can be separated from each other by hand, and there is no need to develop a separation technique as claimed in the present invention for such polymeric beads. To the contrary, the tagging scheme of the present invention provides a substantial improvement in the art by enabling the physical separation of tagged compounds or molecules that are intimately mixed on the molecular level. There is absolutely no disclosure or suggestion in Hochlowski et al. of physical separation of mixed compounds based upon differences in tagging moieties attached thereto. Indeed, the disclosure of Hochlowski et al. is irrelevant to the present invention.

Once again, the Examiner is incorrect in asserting that the term "separate" as used in the present claims encompasses the definition "to discriminate or differentiate between", as, for example, evidenced by Webster's Dictionary. One skilled in the art of the present invention would not give the terms "separating" or "separation" as used in the present claims the definition provided by the Examiner. Indeed, Hawley's Condensed Chemical Dictionary, Thirteenth Edition, R. J. Lewis, editor, Van Norstrand Reinhold, New York, New York (1997) provides a more appropriate definition of the term

"separation" as used in the relevant art as: "A collective term including a large number of unit operations that, in one way or another, isolate the various components of a mixture." This definition of "separation" is not a special definition as asserted by the Examiner, but the common definition of separation in the relevant art. Applicants, have amended the claims to indicated that the separation of the present invention is a "physical separation" and not a mere identification or discrimination as disclosed in Hochlowski et al. This limitation was inherent in the use of the term "separation" in the present specification and claims as originally filed, and this amendment does not change the scope of the claims or any equivalents thereto. Hochlowski et al. does not disclose or suggest a physical separation of the polymeric beads thereof based upon differences in the tags attached thereto.

The Examiner also rejected Claims 1, 2, 3, 10-16 and 45 under 35 U.S.C. 103(a) "as being unpatentable over Curran et al (US 5,859,247; of record) and Hochlowski et al (US 6,168,913), as set forth above". Specifically, the Examiner asserted that:

> Curran et al teach separation techniques where "organic/fluorous phase separation techniques are used to effect separations" (see Abstract). These techniques are defined in column 3, line 35 - column 4, line 4 of the reference and read on the separations of instant claims 1, 2, 11, 12, 14 and 15, especially with respect to tagging moieties that differ in fluorous content. Fluorous reversed phase chromatography is specifically described, column 3, line 49 - column 4, line 4 (reading on claims 3, 13 and 16). Curran et al teach that these methods are preferred for separations (and synthesis) of combinatorial libraries (see column 8, line 50 - column 9, line 32). The reference also teaches that a "plurality of fluorous moieties" can be used "such that any fluorous reaction components . . . are separable from the target organic product" (column 6, lines 29-43) and that "it may be desirable to have more than one tag per molecule, and these tags may be the same or different" (column 16, lines 49-50).
>
> Curran et al lacks the specific teaching of using multiple fluorous tags and separations based on differences between them.

However, the use of multiple tags in the synthesis and analysis of combinatorial libraries was well established in the art at the time of filing. For example, Hochlowski et al teaches "coding combinatorial chemical libraries synthesized on a plurality of solid supports by attaching "tags" that comprise fluorine containing compounds in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine nuclear magnetic resonance spectroscopy..." (see Abstract). Various fluorine containing tags are taught by the reference (see column 5, line 15 through column 13, line 21); these read directly on the claimed fluorous {tagging} moieties that differ in fluorous content or structure of instant claims 2, 12 and 15.

Hochlowski et al teaches using FNMR to identify the tags (see, for example, column 3, lines 2-21 and column 23, lines 1-14), creating for each solid support a code that generates "an unique FNMR spectrum" (column 4, lines 410). Thus, Hochlowski et al clearly teaches differentiating between the tagged library members using their FNMR spectrum (see, for example, column 23, lines 1-14, Example 2 and patented claims). The differentiation discussed above is based on differences between the FNMR chemical shifts of the tagging moieties, see column 5, line 15 through column 13, line 21 {especially column 5, line 29} and Figures. This also reads on the "differences in fluorous nature" in instant claims 1, 11 and 14 and also on the "differences between the first tagging moiety and the second tagging moiety" in instant claim 45. Lastly, as the chemical shifts of the tags are known, the "order" of separation (i.e. placement of peaks in the FNMR spectrum) to identify the compounds that are tagged is deemed to be "predetermined", as recited in instant claims 10 and 45.

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use multiple fluorous tags in the fluorous separations (i.e. reversed phase chromatography) of Curran et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Hochlowski et al regarding the use of multiple fluorine containing tags in order to separate and identify each library compound (see column 2, line 65 through column 3, line 21). Also, the methodology of Curran is advantageous for combinatorial synthesis and analysis for a variety of reasons (see column 8, line 28 through column 9, line 11), such as allowing for reactions to be conducted in homogeneous phases. One would have been further motivated and had a high expectation of success because the tags of both Curran et al and Hochlowski et al are fluorine containing compounds.

The Examiner further indicated that the Applicants' argument filed April 30, 2003 were not persuasive, asserting that:

> In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).
>
> The examiner's position with respect to Hochlowski et al is set forth above. Applicant argues that "Curran et al. does not disclose or suggest the tagging of multiple organic compounds with different fluorous tags" (Response, page 11). The examiner agrees, as it was stated in the rejection that "Curran et al lacks the specific teaching of using multiple fluorous tags and separations based on differences between them." The rejection is based on the *combination* of Curran et al with Hochlowski et al.
>
> As stated in the rejection, the use of multiple tags in the synthesis and analysis of combinatorial libraries was well established in the art at the time of filing. For example, Hochlowski et al teaches "coding combinatorial chemical libraries synthesized on a plurality of solid supports by attaching "tags" that comprise fluorine containing compounds in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine nuclear magnetic resonance spectroscopy..." (see Abstract). Various fluorine containing tags are taught by the reference (see column 5, line 15 through column 13, line 21); these read directly on the claimed fluorous {tagging}moieties that differ in fluorous content or structure of instant claims 2, 12 and 15. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use multiple fluorous tags in the fluorous separations (i.e. reversed phase chromatography) of Curran et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Hochlowski et al regarding the use of multiple fluorine containing tags in order to separate and identify each library compound (see column 2, line 65 through column 3, line 21).

Applicants respectfully traverse the Examiner's rejection.

Curran et al. discloses the separation of a compound that has been tagged with a fluorous moiety from other non-fluorous, organic compounds. As

admitted by the Examiner, Curran et al. does not disclose or suggest the tagging of multiple organic compounds with different fluorous tags to effect a fluorous separation of such fluorous-tagged compounds as set forth in the present invention. Moreover, for the reasons set forth above Hochlowski et al. does not overcome the deficiencies of Curran et al. In that regard, one cannot arrive at the present invention by combining the disclosure of Curran et al. with the disclosure of Hochlowski et al. Once again, Hochlowski et al. uses tags containing fluorine merely to identify different polymeric beads using FNMR. Nowhere does, Hochlowski et al disclose or suggest a physical separation of such polymer beads based upon tags attached thereto.

The Examiner further rejected, claims 1, 2, 3, 10, 11-16 and 45 under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 1-9 of US 5,859,247 (of record) in view of Hochlowski et al (US 6,168,913)". Specifically, the Examiner asserted that:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited claims in the patent and in the instant application encompass separations based on differences in fluorous nature. The instant method uses more than one tagging moiety, while the method of US 5,859,247 only recites one tagging moiety. However, the method instantly claimed would be obvious over that in claims 1-9 of US 5,859,247 because to use more than one tagging moiety (to aid in the separation) would be obvious to one of ordinary skill. This is demonstrated by the teachings of Hochlowski et al, which teach the differentiation of library members using a plurality of fluorine containing tags (see Abstract and column 5, line 15 through column 13, line 21).
>
> Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use multiple fluorous tags in the fluorous separations of Curran et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Hochlowski et al regarding the use of multiple fluorine containing tags in order to separate and identify each library compound (see column 2, line 65 through column 3, line 21). One would have been further motivated and had a high

> expectation of success because the tags of both Curran et al and Hochlowski et al are fluorine containing compounds.

The reply to Applicant's arguments filed April 30, 2003 the Examiner asserted that "Applicant argues that the double patenting rejection is improper for the same reasons that the rejections under 35 USC 102 and 103 are improper. The examiner respectfully disagrees for the reasons set forth in paragraphs 7-9 and 14-16". For the reasons set forth above, Applicants respectfully traverse the Examiner's rejection. Once again, the deficiencies of Curran et al. are not overcome by the disclosure of Hochlowski et al.

The Examiner has also rejected claim 45 under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention". Specifically, the Examiner asserted that:

> Amended claim 45 recites in step b. 'the first fluorous tagging moiety being different from the first fluorous tagging so that....' This phrase is confusing and thus renders the claim indefinite.

Applicants have amended claim 45 to correct a clear typographical error and thereby obviate the Examiner's rejection. In that regard, claim 45 has been amended to indicate "the *second* fluorous tagging moiety being different from the first fluorous tagging moiety." Applicants respectfully assert that claim 45, as amended, fully complies with the requirements of Section 112. This amendment is solely to correct a clear typographical error in Claim 45 and does not affect the scope of the claim or any equivalents thereto.

In view of the above amendments and remarks, the Applicants respectfully requests that the Examiner, indicate the allowability of claims 1-3, 10-16 and 45, and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,

DENNIS P. CURRAN ET AL

By Henry E. Bartony Jr.

Henry E. Bartony, Jr., Esq.
Reg. No. 34,772

Bartony & Hare, LLP
Law & Finance Building
Suite 1801
429 Fourth Avenue
Pittsburgh, Pennsylvania 15219
412-338-8632 (telephone)
412-338-6611 (fax)

Attorney for Applicant